

Treating Type 2 Diabetes with Dietary Supplements

Key Points

- There is limited scientific evidence on the effectiveness of dietary supplements as complementary and alternative medicine (CAM) for type 2 diabetes. The evidence that is available is not sufficiently strong to prove that any of the six supplements discussed in this report have benefits for type 2 diabetes or its complications. A possible exception may be the use of omega-3 fatty acids to lower triglyceride* levels.
- It is very important not to replace conventional medical therapy for diabetes with an unproven CAM therapy.
- To ensure a safe and coordinated course of care, people should inform their health care providers about any CAM therapy that they are currently using or considering.
- The six dietary supplements reviewed in this report appear to be generally safe at low-to-moderate doses. However, each can interact with various prescription medications, affecting the action of the medications. People with type 2 diabetes need to know about these risks and discuss them with their health care provider. Prescribed medicines may need to be adjusted if a person is also using a CAM therapy.

1. What is diabetes?

Diabetes is a chronic condition in which the body cannot properly convert food into energy. Most food that a person eats is eventually broken down into <u>blood</u> <u>glucose</u> (also called blood sugar), which cells need for energy and growth. Insulin is a <u>hormone</u> that helps glucose enter cells. In people with diabetes, the body does not make enough insulin, or it does not respond to insulin properly. This causes glucose to build up in the blood instead of moving into the cells. The most common type of diabetes is type 2 diabetes (formerly called adult-onset diabetes or noninsulin-dependent diabetes). People can develop type 2 diabetes at any age, even in childhood.



Terms that are underlined are defined in the dictionary at the end of this report.

The symptoms of diabetes include fatigue, nausea, a need to urinate frequently, excessive thirst, weight loss, blurred vision, frequent infections, and sores that do not heal. However, some people with diabetes do not have any symptoms. Over time, the high blood glucose levels caused by diabetes can lead to complications in the eyes, blood vessels, nerves, kidneys, feet, teeth, skin, and, especially, the heart. Such complications can be prevented or delayed by keeping blood glucose, blood pressure, cholesterol, and triglycerides in a normal or close-to-normal range.

Some people develop a condition called insulin resistance before they develop type 2 diabetes. When insulin resistance is present, the body does not respond properly to the insulin it has released to lower blood glucose. So, the pancreas releases more insulin to try to keep up with the excess glucose. If the pancreas cannot produce enough insulin, over time this leads to type 2 diabetes. Obesity, aging, and lack of exercise can all play a role in developing insulin resistance and heightening the risk for diabetes.

To find out more about diabetes and related conditions, contact the National Diabetes Information Clearinghouse (see "For More Information").

2. How is diabetes managed in conventional medicine?

In conventional medicine's[†] approach, people with diabetes learn to keep their blood glucose in as healthy a range as possible. They do this by following a healthy food plan, being physically active, controlling their weight, and testing their blood glucose regularly. Some people also need to take medicine, such as insulin injections or prescription diabetes pills. When lifestyle changes and medical treatment are combined to rigorously maintain and control blood sugar in the normal range, this approach to managing type 2 diabetes minimizes the serious complications of the disease. This enables patients to lead productive, full lives.

3. What CAM therapies are discussed in this report?

There are many different CAM therapies used for diabetes and its complications, and it is beyond the scope of this report to discuss them all. Scientific information on any CAM therapy for diabetes can be sought in the PubMed database on the Internet and from the National Center for Complementary and Alternative Medicine (NCCAM) Clearinghouse (for both, see "For More Information"). Overall, there have been few rigorous studies published on the use of CAM approaches for type 2 diabetes. Most of the literature has looked at herbal or other dietary supplements (see box on page 3), which reflects the tradition in certain whole medical systems of using plant products with claimed effects on blood sugar. This report focuses on six of the dietary supplements that people try for diabetes: alpha-lipoic acid (ALA), chromium, coenzyme Q10,

medicine are also practitioners of CAM.

[†] Conventional medicine is medicine as practiced by holders of M.D. (medical doctor) or D.O. (doctor of osteopathy) degrees and by their allied health professionals, such as nurses, physical therapists, and dietitians. Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine. Complementary medicine is used *along with* conventional medicine, and alternative medicine is used *instead of* conventional medicine. Some practitioners of conventional

garlic, magnesium, and omega-3 fatty acids. Discussions of the research findings on these supplements begin in Question 5.

About Dietary Supplements

Dietary supplements were defined in a law passed by Congress in 1994. A dietary supplement must meet all of the following conditions:

- It is a product (other than tobacco) intended to supplement the diet, which contains one or more of the following: vitamins; minerals; herbs or other botanicals; amino acids; or any combination of the above ingredients.
- It is intended to be taken in tablet, capsule, powder, softgel, gelcap, or liquid form.
- It is not represented for use as a conventional food or as a sole item of a meal or the diet.
- It is labeled as being a dietary supplement.

Other important information about dietary supplements:

- They are regulated as foods, not drugs, so there could be quality issues in the manufacturing process.
- Supplements can interact with prescribed or over-the-counter medicines, and other supplements.
- "Natural" does not necessarily mean "safe" or "effective."
- Consult your health care provider before starting a supplement, especially if you are pregnant or nursing, or considering giving a supplement to a child.

4. What should people do if they have diabetes and are considering using any CAM therapy?

- People with diabetes need to be under the care of a physician or other health care provider
 who will help them learn to manage their diabetes and will monitor their efforts to control it.
 Dietitians and diabetes educators help people learn and use the skills needed for managing
 diabetes on a daily basis. In addition, many patients need to be under the care of one or more
 specialists, such as an endocrinologist, an ophthalmologist, and/or a podiatrist.
- It is important to not replace scientifically proven treatments for diabetes with CAM treatments that are unproven. The consequences of not following one's prescribed medical regimen for diabetes can be very serious, even life-threatening.
- People with diabetes should tell their health care provider about any dietary supplements or medications (prescription or over-the-counter) that they are using or considering. Prescribed medicines for diabetes and all other major health conditions may need to be adjusted if a

person is also using a CAM therapy. Pharmacists can be another helpful source of information about dietary supplements.

- If they decide to use supplements, they should know that what they see on the label may not
 accurately reflect what is in the bottle. Some herbal supplements, for example, have been found
 to be contaminated; some tests of dietary supplements have found that the contents did not
 match the labeled dose on the bottle. The NCCAM Clearinghouse (see "For More Information")
 has publications on this topic.
- Women who are pregnant or nursing, or people who are thinking of using supplements to treat a child, should use extra caution and be sure to consult their health care provider.
- If people with diabetes decide to use a supplement and notice any unusual effects, they should stop and contact their health care provider.
- 5. What is known about the safety and effectiveness of these six dietary supplements as CAM treatments for diabetes?

Below is a brief overview of each dietary supplement and what is known from research about its effectiveness and safety in use for diabetes.

Alpha-Lipoic Acid

Alpha-lipoic acid (ALA, also known as lipoic acid or thioctic acid) is a chemical that is similar to a vitamin. It is an antioxidant—a substance that prevents cell damage caused by substances called <u>free radicals</u> in a process called oxidative stress. High levels of blood glucose are one cause of oxidative stress. ALA is found in some foods, such as liver, spinach, broccoli, and potatoes. ALA can also be made in the laboratory. ALA supplements are marketed as tablets or capsules.[‡] It is theorized that ALA may be beneficial because of its antioxidant activity.

Summary of the research findings

The evidence on ALA for type 2 diabetes and obesity is limited. There are a number of small studies in animals and in people that have shown hints of beneficial effects. In a few of these studies, some possible benefit from ALA was seen in glucose uptake in muscle; sensitivity of the body to insulin; diabetic neuropathy; and/or weight loss. More research is needed to document whether there is any benefit of ALA in diabetes and to better understand how ALA works.

Side effects and possible risks

While ALA appears to be safe for the general adult population, people with diabetes need to know that ALA might lower blood sugar too much, and thus they would need to monitor their blood sugar level especially carefully. ALA may also lower blood levels of minerals, such as iron; interact with some medicines, such as antacids; and decrease the effectiveness of some anti-cancer drugs. Other possible side effects of ALA include headache, skin rash, and stomach upset.

[‡] There is some use, reported from outside the United States, of ALA delivered intravenously (IV). These trials are not discussed in this report.

Chromium

Chromium is a metal and an <u>essential trace mineral</u>. Chromium is found in some foods, such as meats, animal fats, fish, brown sugar, coffee, tea, some spices, whole-wheat and rye breads, and brewer's yeast. It is marketed in supplement form (capsules and tablets) as chromium picolinate, chromium chloride, and chromium nicotinate.

Summary of the research findings

There are scientific controversies about the use or need for chromium supplementation by persons with diabetes. First, it is difficult to determine, including through tests, whether a person has a chromium deficiency. Second, it is not known whether it is beneficial to take chromium supplementation in diabetes, and there is a lack of rigorous <u>basic science studies</u> to explain or support any evidence of benefit. In sum, there is not enough evidence to show that taking chromium supplements is beneficial for diabetes.

Side effects and other risks

At low doses, short-term use of chromium appears to be safe in the general adult population. However, chromium can add to insulin in its effects on blood sugar; this might cause the blood sugar to go too low. Possible side effects at low doses include weight gain, headache, insomnia, skin irritation, sleep problems, and mood changes. High doses can cause serious side effects. The foremost concern for persons with diabetes who use chromium is the development of kidney problems. Other possible effects include vomiting, diarrhea, bleeding into the gastrointestinal tract, and worsening of any behavioral or psychiatric problems.

Coenzyme Q10

Coenzyme Q10, often referred to as CoQ10 (sometimes written as CoQ_{10} ; other names include ubiquinone and ubiquinol) is a vitamin-like substance. CoQ10 helps cells make energy and acts as an antioxidant. Meats and seafood contain small amounts of CoQ10. Supplements are marketed as tablets and capsules.

Summary of the research findings

There have been few studies on CoQ10 and type 2 diabetes so far. The evidence is not sufficient to evaluate CoQ10's effectiveness as a CAM therapy in diabetes. CoQ10 has not been shown to affect blood glucose control. In theory, it might have use against heart disease in people with diabetes, but well-designed studies looking at heart disease outcomes are needed to answer this question.

Side effects and other risks

CoQ10 appears to be safe for most of the adult population. However, it may interact with and affect the action of some medicines, including warfarin (a blood thinner) and medicines used for high blood pressure or cancer chemotherapy. Other possible side effects of CoQ10 include nausea, vomiting, diarrhea, loss of appetite, and heartburn.

Garlic

Garlic (Allium sativum) is an herb used to flavor food. Garlic can also be processed and made into dietary supplements. In some cultures, garlic is used for medicinal purposes. The chemical in garlic of most interest for health purposes is allicin, which gives garlic its strong taste and odor. One of the claims for garlic is that the rates of certain diseases are lower in countries where lots of garlic is consumed. However, it has not been proven that garlic (and not some other factor such as lifestyle) is the reason.

Summary of the research findings

Few rigorous studies have been conducted on garlic, allicin, or both, for type 2 diabetes. In the studies that have been done, findings have been mixed. There are some intriguing basic science studies that suggest that garlic has some biological activities that are relevant to the treatment of diabetes. However, the evidence so far does not support that there is any benefit from garlic for type 2 diabetes.

Side effects and other risks

Garlic is safe for most adults. However, garlic appears to interact with various types of drugs. For example, when combined with certain medicines used to treat HIV/AIDS (NNRTIs and saquinavir), garlic may decrease their effectiveness. Garlic may also interact with and affect the action of birth control pills, cyclosporine, medications that are broken down by the liver, and blood thinners (including warfarin). Other possible side effects of garlic include an odor on the breath or skin, an allergic reaction, stomach disorders, diarrhea, and skin rash.

Magnesium

Magnesium is a mineral. Foods high in magnesium include green leafy vegetables, nuts, seeds, and some whole grains. Various supplemental forms of magnesium are marketed as tablets, capsules, or liquids.

Magnesium has many important functions in the body, including in the heart, nerves, muscles, bones, handling glucose, and making proteins. Low levels of magnesium are commonly seen in people with diabetes. Scientists have studied the relationship between magnesium and diabetes for a long time, but it is not yet fully understood.

Summary of the research findings

There have been a handful of studies on magnesium and type 2 diabetes, many of them very small in size and/or short in length and primarily looking at blood glucose control. The results have been mixed, with most finding that magnesium did not affect blood glucose control. Some studies have suggested that low magnesium levels may make glucose control worse in type 2 diabetes (interrupting insulin secretion in the pancreas and increasing insulin resistance) and contribute to diabetes complications. There is evidence that magnesium supplementation may be helpful for insulin resistance. Additional controlled studies are needed to establish firmly whether magnesium supplements have any role or benefit as a CAM therapy for type 2 diabetes.

Side effects and other risks

Magnesium supplements appear to be safe for most adults at low doses. High doses can be unsafe and cause such problems as nausea, diarrhea, loss of appetite, muscle weakness, difficulty breathing, extremely low blood pressure, irregular heart rate, and confusion. Magnesium can interact with and affect the action of certain drugs, including some antibiotics, drugs to prevent osteoporosis, certain high blood pressure medicines (calcium channel blockers), muscle relaxants, and diuretics ("water pills").

Omega-3 Fatty Acids

Omega-3 fatty acids (omega-3s, for short) are a group of <u>polyunsaturated fatty acids</u> that come from food sources, such as fish, fish oil, some vegetable oils (primarily canola and soybean), walnuts, wheat germ, and certain dietary supplements. As supplements, omega-3s are marketed as capsules or oils, often as fish oil.

Omega-3s are important in a number of bodily functions, including moving calcium and other substances in and out of cells, the relaxation and contraction of muscles, blood clotting, digestion, fertility, cell division, and growth. Omega-3s have been the subject of much media attention in recent years, because of studies finding they may be useful for such purposes as decreasing the rate of heart disease, reducing inflammation, and lowering triglyceride levels. Some countries and organizations have issued formal recommendations on the intake of omega-3s, through meals, oils, and possibly supplementation. Omega-3s have been of interest for diabetes primarily because having diabetes increases a person's risk for heart disease and stroke.

Summary of the research findings

<u>Randomized clinical trials</u> have found that omega-3 supplementation reduces the incidence of cardiovascular disease and events (such as heart attack and stroke) and slows the progression of atherosclerosis (hardening of the arteries). However, these studies were not done in populations that were at higher risk, such as those with type 2 diabetes.

With regard to studies on omega-3 supplementation for type 2 diabetes, there is somewhat more literature available than for most other CAM therapies for this condition. A 2001 analysis was published by the Cochrane Collaboration, of 18 randomized <u>placebo-controlled trials</u> on fish oil supplementation in type 2 diabetes. The authors found that fish oil lowered triglycerides and raised LDL cholesterol but had no significant effect on <u>fasting blood glucose</u>, <u>HbA1c</u>, total cholesterol, or HDL cholesterol. (The authors did not identify and include studies with cardiovascular outcomes, but noted that this is an area for further research.) Another analysis was published in 2004 by the Agency for Healthcare Research and Quality, of 18 studies on omega-3 fatty acids for a number of measurable outcomes in type 2 diabetes. This study confirmed virtually all the Cochrane authors' findings, except for finding no significant effect on LDL cholesterol.

Additional studies are needed to determine whether omega-3 supplements are safe and beneficial for heart problems in people with type 2 diabetes. Studies that look specifically at heart disease outcomes in this population are needed.

Side effects and possible risks

Omega-3s appear to be safe for most adults at low-to-moderate doses. There have been some safety questions raised about fish oil supplements, because certain species of fish can be contaminated with substances from the environment, like mercury, pesticides, or <u>PCBs</u>. Fish oil is on the list of food substances that the U.S. Food and Drug Administration considers to be "generally recognized as safe." How well a product is prepared is another factor for consumers to consider. Women who are pregnant or breastfeeding should not take fish oil supplements. Fish oil in high doses can possibly interact with, and affect the action of, certain medications, including blood-thinning drugs and drugs for high blood pressure. Potential side effects of fish oil include a fishy aftertaste, belching, stomach disturbances, and nausea.

6. What research is being done on CAM therapies for diabetes?

Recent NCCAM-supported research projects are studying the effects of:

- Chromium on high blood glucose levels
- Yoga on glucose control in people at risk for diabetes
- Ginkgo biloba extract on diabetes medicines

Also, researchers in the Diabetes Unit of NCCAM's Division of Intramural Research are studying many aspects of diabetes, including what happens when the body does not properly react to insulin. Recent clinical trials, for example, have been studying whether vitamin C supplements are beneficial in diabetes, the safety of glucosamine with respect to insulin resistance, and whether dark chocolate lowers blood pressure and improves insulin sensitivity. Diabetes Unit staff note that a category of <u>functional foods</u> containing <u>polyphenols</u> (also available as extracts) may be of benefit for further study in diabetes, including green tea (epigallocatechin gallate), dark chocolate (epicatechin), and red wine (resveratrol).

Definitions

Basic science study: A laboratory study done at the molecular level of biology and/or chemistry, to obtain necessary knowledge and background for later research such as animal studies and clinical trials.

Blood glucose: The main sugar found in the blood. Glucose serves as the body's primary source of energy.

Clinical trial: A research study in which a treatment or therapy is tested in people to see whether it is safe and effective. Clinical trials are a key part of the process in finding out which treatments work, which do not, and why. Clinical trial results also contribute new knowledge about diseases and medical conditions.

Controlled study: A clinical trial in which one group receives a treatment under study and another group (the control group) receives either a placebo, standard treatment, or no treatment.

Diabetic neuropathy: A nerve disorder caused by diabetes. This disorder leads to pain or loss of feeling in the toes, feet, legs, hands, or arms.

Endocrinologist: A specialist in diseases and conditions of the glands (organs that make hormones).

Essential trace mineral: A mineral that is required in minute amounts by the body and must be obtained from dietary sources.

Fasting blood glucose: Blood glucose level after a person has not eaten for 8 to 12 hours (usually overnight).

Free radical: A highly reactive chemical that attacks molecules that are key to cell functioning, by capturing electrons and thus changing chemical structures.

Functional food: A food that has biologically active components (such as fish oils or plant estrogens) that may provide health benefits beyond basic nutrition.

HbA1c: Hemoglobin A1c, a blood test that measures a person's average blood glucose level over a period of weeks or months.

Hormone: A chemical made by glands in the body. Hormones circulate in the bloodstream and control the actions of certain cells or organs. Some hormones can also be made in laboratories.

Ophthalmologist: A specialist in diseases and disorders of the eye.

PCB: Short for polychlorinated biphenyl. PCBs have had various uses in industry, but most uses were banned by the U.S. Environmental Protection Agency in 1979 because of hazards to human health. When discharged into the environment, PCBs stay in the environment for a long period of time and build up in certain species of fish and wildlife.

Placebo: An inert or sham treatment, such as a sugar pill.

Podiatrist: A specialist in care of the foot and treatment of foot disorders.

Polyphenols: A group of substances that are found in many plants. They give some flowers, fruits, and vegetables their color. Polyphenols have antioxidant activity and are being studied as possible CAM treatments.

Polyunsaturated fatty acid: One of the three types of fatty acids. Polyunsaturated fatty acids are liquid at room temperature. They contain a chain of carbon atoms and hydrogen and oxygen molecules, with two or more double bonds between the carbon atoms.

Randomized clinical trial: In a randomized clinical trial, each participant is assigned by chance (through a computer or a table of random numbers) to one of two groups. The investigational

group receives the therapy, also called the active treatment. The control group receives either the standard treatment, if there is one for their disease or condition, or a placebo.

Triglyceride: The form in which fat is stored in the body. High triglyceride levels in the blood may raise the risks for heart attack or stroke.

Whole medical system: A system that employs practices from among the four CAM domains—mind-body medicine, biologically based practices, manipulative and body-based practices, and energy medicine. Conventional medicine is one example of a whole medical system. An example of a CAM whole medical system is traditional Chinese medicine.

Sources

Question 1: References 1-4

Question 2: References 1, 3-5

Question 3: N/A

Question 4: N/A

Question 5:

Alpha-lipoic acid: References 6-13

• Chromium: References 11, 14-18

• Coenzyme Q10: References 7, 19-21

• Garlic: References 11, 22-28

• Magnesium: References 11, 15, 29-33

• Omega-3 fatty acids: References 34-42

Question 6: N/A

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For More Information

NCCAM Clearinghouse

The NCCAM Clearinghouse provides information on CAM and on NCCAM, including publications and searches of Federal databases of scientific and medical literature. The Clearinghouse does not provide medical advice, treatment recommendations, or referrals to practitioners.

Toll-free in the U.S.: 1-888-644-6226

TTY (for deaf and hard-of-hearing callers): 1-866-464-3615

Web site: nccam.nih.gov E-mail: info@nccam.nih.gov

National Diabetes Information Clearinghouse

A service of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health (NIH), the clearinghouse responds to inquiries, offers diabetes publications, makes referrals, and maintains the diabetes subfile of the Combined Health Information Database (chid.nih.gov).

Toll-free in the U.S.: 1-800-860-8747 Web site: www.diabetes.niddk.nih.gov

National Diabetes Education Program

The National Diabetes Education Program is a program sponsored by NIH and the Centers for Disease Control and Prevention, with many Federal, state, and local partners. Among its services are information and publications.

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Created June 2, 2005 D267